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EXAMINER	
NOGUEROLA, ALEXANDER STEPHAN	

ART UNIT	PAPER NUMBER
1753	

DATE MAILED: 06/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/636,104	WANG ET AL.	
	Examiner	Art Unit	
	ALEX NOGUEROLA	1753	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,11-18,20,23-25,28,32-34,36,37,40,41,43-48,50-69,72 and 73* is/are pending in the application.

4a) Of the above claim(s) *53-67* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,11-18,20,23-25,28,32-34,36-38,40,41,43-48,50-52,68,69,72 and 73* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 August 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Rejections Pending since the Office action of December 23, 2004

1. All previous rejections are withdrawn.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-8, 11-18, 20, 23-25, 28, 32-34, 36-38, 40, 41, 43-48, and 50-52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention:

a) Claim 1, line 5: -- microlfuidic application -- should be inserted before "chip";

b) Claim 1, line 7: Does "built-in in" mean -- built into --?

c) Claim 45: Applicants stated they deleted limitation (b)(viii) from claim 1 in order to overcome Weetall (see page 15 of the Amendment of March 23, 2005);

however claim 45 retains this limitation. Thus, claim 45 is indefinite because it is not clear whether Applicants inadvertently forgot to cancel claim 45.

4. Note that dependent claims will have the deficiencies of base and intervening claims.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims1-8, 12-18, 23-25, 28, 32, 40, 41, 48, 50-52, 68, and 69 are rejected under 35 U.S.C. 102(e) as being anticipated by Parton et al. (US 5,993,631) ("Parton").

Addressing claims 1, 40, 41, and 48, Parton discloses a method for manipulating a moiety in a microfluidic application, which method comprises

a) coupling a moiety to be manipulated onto a surface of a binding partner of the moiety to form a moiety-binding partner complex (see Figures 9-12. Note in Figures 9-12 either the microparticle or the dielectric label can be construed as the binding partner); and

b) manipulating the moiety-binding partner complex with a physical force in a chip format, wherein the manipulation is effected through a combination of a signal source that is external to the chip and a structure that is built-in in the chip, thereby the moiety is manipulated (abstract and Figure 7), and wherein

the moiety is not directly manipulatable by a dielectrophoresis force and the moiety binding partner complex is manipulated by a dielectrophoresis force (inherent since claim 7 allows for the moiety to be protein or a nucleic acid and claim 12 allows for the binding partner to be a plastic particle. Parton discloses proteins and nucleic acids as moieties and plastic/polymer binding partners. See col. 3:10-12; col. 3:13-25; col. 9:42-47; and col. 3:61 - col. 4:10. Also note that Parton discloses that the binding partner may be a magnetic bead or a metal particle, which is also included in the Markush group of claim 12).

Although not needed to meet claim 1, Applicants should note that Parton also discloses that the moiety is not directly manipulatable by a traveling wave force and the moiety binding partner complex is manipulated by a traveling wave force. See the Parton abstract and the immediately preceding paragraph.

Addressing claims 2-7, for the additional limitations of these claims see col. 5:1-5; Figures 9 and 10; and col. 3:1-12. For claim 6 note that claim 5 does not require the molecule to be an inorganic molecule. The molecule could still be an organic molecule or a complex of an organic molecule and an inorganic molecule.

Addressing claim 8, for the additional limitation of this claim see Figures 9 and 10

Addressing claim 12, for the additional limitation of this claim see col. 3:61 - col. 4:10 and col. 3:1-9.

Addressing claim 13, for the additional limitation of this claim see Figures 9-12.

Addressing claim 14, for the additional limitation of this claim see Figures 10 and 11. a nucleic acid strand can be cleaved from a complementary strand by denaturing. A nucleic acid strand may itself be cleaved with an appropriate enzyme.

Addressing claims 15-18, for the additional limitations of these claims see Figures 9-12. Note that nucleic acid strand can be cleaved from a complementary strand by denaturing (physical treatment or chemical treatment (heat or pH)). A nucleic acid strand may itself be cleaved with an appropriate enzyme.

Addressing claim 20, for the additional limitation of this claim see Figures 1-7 and 13.

Addressing claims 23-25; claim 1 does not necessarily require an acoustic force or an electrostatic force. These forces are only in the alternative, along with dielectrophoresis force and traveling wave force, which Parton discloses.

Addressing claim 28, for the additional limitation of this claim see col. 6:50-52.

Addressing claim 32, for the additional limitation of this claim see col. 6:58-65.

Addressing claims 50 and 51, Parton discloses sorting chromosomes, for example, using pre-labeled dielectric markers. See col. 10:8-12.

Addressing claim 52, since the moities must be separated sequentially or simultaneously one or the other occurs in Parton. Alternatively, the example of sorting chromosomes implies simultaneous sorting. Alternatively, since Parton discloses an embodiment in which antibodies are sorted and an embodiment in which chromosomes are sorted Parton also discloses sequential sorting of different moities. See Figures 8-12.

Addressing claim 68, Parton discloses a kit for manipulating a moiety in a microfluidic application, which kit comprises

a) a binding partner onto the surface of which a moiety to be manipulated can be coupled to form a moiety-binding partner complex (Figures 9-12. Note hat either the microparticle or the dielectric label can be construed as a binding partner);

b) means for coupling the moiety onto the surface of the binding partner (Figures 9-12);

c) a chip on which the moiety-binding partner complex can be manipulated with a physical force that is effected through a combination of a signal source that is external to the chip and a structure that is built-in in the chip, thereby the moiety is manipulated (abstract and Figure 7), and wherein

the moiety is not directly manipulatable by a dielectrophoresis force and the moiety binding partner complex is manipulated by a dielectrophoresis force (inherent since claim 7 allows for the moiety to be protein or a nucleic acid and claim 12 allows for the binding partner to be a plastic particle. Parton discloses proteins and nucleic acids as moieties and plastic/polymer binding partners. See col. 3:10-12; col. 3:13-25; col. 9:42-47; and col. 3:61 - col. 4:10. Also note that Parton discloses that the binding partner may be a magnetic bead or a metal particle, which is also included in the Markush group of claim 12).

Although not needed to meet claim 68, Applicants should note that Parton also discloses that the moiety is not directly manipulatable by a traveling wave force and the moiety binding partner complex is manipulated by a traveling wave force. See the Parton abstract and the immediately preceding paragraph.

Addressing claim 69, Parton discloses a method as required by claim 68. See the rejection of claim 69 under 35 U.S.C. 102(e), above. Although Parton does not mention providing instructions for coupling the moiety onto the surface of the binding partner and/or manipulate the moiety-binding partner complex on the chip, it would have been obvious to one with ordinary skill in the art at the time the invention was made to do so because then the operator of the kit will have to lose less time with trial and error experiments on how to use the kit.

7. Claims 45, 68, and 69 are rejected under 35 U.S.C. 102(b) as being anticipated by Weetall et al. (US 5,620,857).

Addressing claims 45 and 68, for the claimed limitations see the abstract; Figure 1; col. 3:32-46; col. 3: 53-59; col. 4: 39-41; col. 5: 45-62; col. 6:15-23, col. 6:60-67 (competitive binding implies cleavable linkage), col. 7:63 – col. 8:3. Note that the structure comprising the cover slip (15) and well (17) at the top of Figure 1 can be construed as the chip of claim 1, the lens shown (but not labeled) in Figure 1 can be construed as the "structure that is built-in in said chip" of claim 1, and the laser of Figure 1 can be construed as the "signal source that is external to said chip." Also, Weetall specifically mentions using a "chip" format. See col. 7:63 to 8:1.

For claim 68 note that since the kit does not require a moiety parts (c) (i-vii) of the claim are only intended uses that do note further structurally limit the claim, especially since some of these alternative limitations have phrases begining with "is manipulated".

Addressing claim 69, Weetall discloses a method as required by claim 68. See the rejection of claim 68 under 35 U.S.C. 102(b), above. Although Weetall does not mention providing instructions for coupling the moiety onto the surface of the binding partner and/or manipulate the moiety-binding partner complex on the chip, it would have been obvious to one with ordinary skill in the art at the time the invention was made to do so because then the operator of the kit will have to lose less time with trial and error experiments on how to use the kit.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 11, 46, and 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Parton et al. (US 5,993,631) ("Parton") in view of Weetall (US 5,620,857) ('Weetall").

Addressing claim 11, Parton discloses a method for manipulating a moiety in a microfluidic application, which method comprises

a) coupling a moiety to be manipulated onto a surface of a binding partner of the moiety to form a moiety-binding partner complex (see Figures 9-12); and

b) manipulating the moiety-binding partner complex with a physical force in a chip format, wherein the manipulation is effected through a combination of a signal source that is external to the chip and a structure that is built-in in the chip, thereby the moiety is manipulated (abstract and Figure 7), and wherein

the moiety is not directly manipulatable by a dielectrophoresis force and the moiety binding partner complex is manipulated by a dielectrophoresis force (inherent

since claim 7 allows for the moiety to be protein or a nucleic acid and claim 12 allows for the binding partner to be a plastic particle. Parton discloses proteins and nucleic acids as moieties and plastic/polymer binding partners. See col. 3:10-12; col. 3:13-25; col. 9:42-47; and col. 3:61 - col. 4:10. Also note that Parton discloses that the binding partner may be a magnetic bead or a metal particle, which is also included in the Markush group of claim 12).

Although not needed to meet the claim, Applicants should note that Parton also discloses that the moiety is not directly manipulatable by a traveling wave force and the moiety binding partner complex is manipulated by a traveling wave force. See the Parton abstract and the immediately preceding paragraph.

Parton does not mention a dimension range for the microparticles, although arguably a dimension within the claimed range is disclosed by Parton since Parton discloses *mic*roparticles.

Weetall discloses using microparticles with a dimension of 0.4 microns in a method for manipulating a moiety in a microfluidic application. See the abstract; and col. 3:32-35 and col. 4:40-41. It would have been obvious to use microparticles sized as those used by Weetall in the invention of Parton or even more broadly within Applicants' claimed range because barring a contrary showing, such as unexpected results, one with ordinary skill in the art at the time of the invention would select the size of the microparticles based on sizes of the analytes and associated coupling agents and labels and the binding capacity of microparticles, and the ability of the manipulating force to accurately manipulate microparticles of different sizes.

Addressing claims 46 and 47, Parton discloses a method for manipulating a moiety in a microfluidic application, which method comprises

a) coupling a moiety to be manipulated onto a surface of a binding partner of the moiety to form a moiety-binding partner complex (see Figures 9-12); and

b) manipulating the moiety-binding partner complex with a physical force in a chip format, wherein the manipulation is effected through a combination of a signal source that is external to the chip and a structure that is built-in in the chip, thereby the moiety is manipulated (abstract and Figure 7), and wherein

the moiety is not directly manipulatable by a dielectrophoresis force and the moiety binding partner complex is manipulated by a dielectrophoresis force (inherent since claim 7 allows for the moiety to be protein or a nucleic acid and claim 12 allows for the binding partner to be a plastic particle. Parton discloses proteins and nucleic acids as moieties and plastic/polymer binding partners. See col. 3:10-12; col. 3:13-25; col. 9:42-47; and col. 3:61 - col. 4:10. Also note that Parton discloses that the binding partner may be a magnetic bead or a metal particle, which is also included in the Markush group of claim 12).

Although not needed to meet the claim, Applicants should note that Parton also discloses that the moiety is not directly manipulatable by a traveling wave force and the moiety binding partner complex is manipulated by a traveling wave force. See the Parton abstract and the immediately preceding paragraph.

Addressing claims 46 and 47, Parton does not mention the claimed ranges for coupled moiety. However, Weetall discloses using a physical force to manipulate a very

wide range of concentrations of coupled moieties ($1.49x10^{-5}$ M to $1.49x10^{-15}$ M). See col. 5:45-52. Thus, barring evidence to the contrary, such as unexpected results, the extent to which moiety is coupled to the surface of the binding partner is a matter of optimizing the method for the detection limit and amount of moiety. See col. 6:15-28 in Weetall.

12. Claims 33 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Parton et al. (US 5,993,631) ("Parton").

Addressing claim 33, Parton discloses a method for manipulating a moiety in a microfluidic application, which method comprises

a) coupling a moiety to be manipulated onto a surface of a binding partner of the moiety to form a moiety-binding partner complex (see Figures 9-12); and

b) manipulating the moiety-binding partner complex with a physical force in a chip format, wherein the manipulation is effected through a combination of a signal source that is external to the chip and a structure that is built-in in the chip, thereby the moiety is manipulated (abstract and Figure 7), and wherein

the moiety is not directly manipulatable by a dielectrophoresis force and the moiety binding partner complex is manipulated by a dielectrophoresis force (inherent since claim 7 allows for the moiety to be protein or a nucleic acid and claim 12 allows for the binding partner to be a plastic particle. Parton discloses proteins and nucleic acids as moieties and plastic/polymer binding partners. See col. 3:10-12; col. 3:13-25; col.

9:42-47; and col. 3:61 - col. 4:10. Also note that Parton discloses that the binding partner may be a magnetic bead or a metal particle, which is also included in the Markush group of claim 12).

Although not needed to meet the claim, Applicants should note that Parton also discloses that the moiety is not directly manipulatable by a traveling wave force and the moiety binding partner complex is manipulated by a traveling wave force. See the Parton abstract and the immediately preceding paragraph.

Parton does not mention "decoupling the moiety from the surface of the binding partner after the moiety is manipulated." It would have been obvious to one with ordinary skill in the art at the time the invention was made to so decouple the moiety because then the binding partner could be reused for another sample containing the same or a different moiety. Decoupling techniques for nucleic acid strands, such as enzymatic cleavage or denaturing were known at the time of the invention and was within the skill of one with ordinary skill in the art.

Addressing claim 36, Parton discloses a method for manipulating a moiety in a microfluidic application, which method comprises

a) coupling a moiety to be manipulated onto a surface of a binding partner of the moiety to form a moiety-binding partner complex (see Figures 9-12); and

b) manipulating the moiety-binding partner complex with a physical force in a chip format, wherein the manipulation is effected through a combination of a signal

source that is external to the chip and a structure that is built-in in the chip, thereby the moiety is manipulated (abstract and Figure 7), and wherein

the moiety is not directly manipulatable by a dielectrophoresis force and the moiety binding partner complex is manipulated by a dielectrophoresis force (inherent since claim 7 allows for the moiety to be protein or a nucleic acid and claim 12 allows for the binding partner to be a plastic particle. Parton discloses proteins and nucleic acids as moieties and plastic/polymer binding partners. See col. 3:10-12; col. 3:13-25; col. 9:42-47; and col. 3:61 - col. 4:10. Also note that Parton discloses that the binding partner may be a magnetic bead or a metal particle, which is also included in the Markush group of claim 12).

Although not needed to meet the claim, Applicants should note that Parton also discloses that the moiety is not directly manipulatable by a traveling wave force and the moiety binding partner complex is manipulated by a traveling wave force. See the Parton abstract and the immediately preceding paragraph.

Parton does not mention having the moiety be mRNA and using oligo-dT polynucleotide for binding. However, Parton clearly discloses a variety of nucleic acids including RNA may be used. See col. 3:10-12. So barring a contrary showing, such as unexpected results, messenger RNA as a moiety is just a matter of being the analtye of interest at the moment. As for oligo-dT polynucleotide, Parton also discloses using a nucleic acid probe with the appropriate affinity and selectivity for the moiety. See col. 3:25-38 and col. 3:46-53.

13. Claim 34 is rejected under 35 U.S.C. 103(a) as being unpatentable over Parton et al. (US 5,993,631) ("Parton") in view of Hawkins (WO 96/09379 A1) ('Hawkins"), CAPLUS abstract of Ma et al. ("Synthesis of uniform microspheres with higher content of 2-hydroxylmethacrylate by employing SPG (Shirasu porous glass) emulsification technique followed by swelling process of droplets," Journal of Applied Polymer Science (1997), 66(7), 1325-1341) ("Ma"), CAPLUS abstract of Chen et al. (CN 1145410 A), and CAPLSU abstract of Yang et al. ("New, porous microsphere of bisphenol A epoxy resin," Gaofenzi Xuebao (1997), (1), 119-120) ("Yang").

Parton discloses a method for manipulating a moiety in a microfluidic application, which method comprises

a) coupling a moiety to be manipulated onto a surface of a binding partner of the moiety to form a moiety-binding partner complex (see Figures 9-12); and

b) manipulating the moiety-binding partner complex with a physical force in a chip format, wherein the manipulation is effected through a combination of a signal source that is external to the chip and a structure that is built-in in the chip, thereby the moiety is manipulated (abstract and Figure 7), and wherein

the moiety is not directly manipulatable by a dielectrophoresis force and the moiety binding partner complex is manipulated by a dielectrophoresis force (inherent since claim 7 allows for the moiety to be protein or a nucleic acid and claim 12 allows for the binding partner to be a plastic particle. Parton discloses proteins and nucleic acids as moieties and plastic/polymer binding partners. See col. 3:10-12; col. 3:13-25; col. 9:42-47; and col. 3:61 - col. 4:10. Also note that Parton discloses that the binding

partner may be a magnetic bead or a metal particle, which is also included in the Markush group of claim 12).

Although not needed to meet the claim, Applicants should note that Parton also discloses that the moiety is not directly manipulatable by a traveling wave force and the moiety binding partner complex is manipulated by a traveling wave force. See the Parton abstract and the immediately preceding paragraph.

Although Parton discloses DNA as a moiety and a bead as a binding partner (see Figures 10 and 11), Parton does not mention having the binding partner be a porous bead and reversibly binding the DNA onto the surface of the bead in a buffer containing high salt concentration.

Hawkins discloses reversibly binding poilynucleotides, such as DNA, onto microparticles in a buffer having a high salt concentration. See page 3:25 – page 4:7 and page 3:20-24. It would have been obvious to one with ordinary skill in the art at the time of the invention to reversibly bind DNA, onto microparticles in a buffer having a high salt concentration as taught by Hawkins in the invention of Parton because then the microparticles can be recovered for use with a new sample and the DNA can be further processed or analyzed in a pure state (uncongugated) after the manipulation.

As for a porous bead, neither Parton nor Hawkins mention whether the bead is porous. However, they disclose that a wide variety of beads may be used (in Parton see col. 4:8-10 and in Hawkins see page 4:19-22) and a variety of porous microbeads were known at the time of the invention. See, for example, Yang, Chen, Ma. So, barring evidence to the contrary, such as unexpected results the choice of bead, such as a

porous bead as taught by Yang, Chen, or Ma is just optimization. On with ordinary skill in the art at the time of the invention would select a bead that is compatible at least with the analyte it is to reversibly bind and the manipulating force. .

14. Claims 37 and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Parton et al. (US 5,993,631) ("Parton") in view of Hawkins (WO 96/09379 A1) ('Hawkins"), CAPLUS abstract of Yuan et al. ("Protein-loaded poly (ε-caprolactone) microparticles. I. Optimization of the preparation by (water-in-oil)-in water emulsion solvent evaporation," journal of Encapsulation 91999), 16(5), 587-599) ('Yuan"), CAPLUS abstract of Rojas et al. ("A polysorbate-based nonionic surfactant can modulate loading and release of (β-lactoglobulin entrapped in multiphase poly(DL-lactide-co-glycolide) microspheres," Pharmaceutical Research (1999), 16(2), 255-260) ("Rojas"), Hernandez et al. ("Influence of shaking and surfactants on the release of BSA from PLGA microspheres," European journal of Drug Metabolism and Pharmacokinetics (1998), 23(2), 92-96) ("Hernandez"), and Shen ("Preparation, characterization and application of magnetic microsphere," Huaxue tongbao (1997), (9), 55-57) ("Shen"). .

Addressing claim 37, Parton discloses a method for manipulating a moiety in a microfluidic application, which method comprises

a) coupling a moiety to be manipulated onto a surface of a binding partner of the moiety to form a moiety-binding partner complex (see Figures 9-12); and

b) manipulating the moiety-binding partner complex with a physical force in a chip format, wherein the manipulation is effected through a combination of a signal source that is external to the chip and a structure that is built-in in the chip, thereby the moiety is manipulated (abstract and Figure 7), and wherein

the moiety is not directly manipulatable by a dielectrophoresis force and the moiety binding partner complex is manipulated by a dielectrophoresis force (inherent since claim 7 allows for the moiety to be protein or a nucleic acid and claim 12 allows for the binding partner to be a plastic particle. Parton discloses proteins and nucleic acids as moieties and plastic/polymer binding partners. See col. 3:10-12; col. 3:13-25; col. 9:42-47; and col. 3:61 - col. 4:10. Also note that Parton discloses that the binding partner may be a magnetic bead or a metal particle, which is also included in the Markush group of claim 12).

Although not needed to meet the claim, Applicants should note that Parton also discloses that the moiety is not directly manipulatable by a traveling wave force and the moiety binding partner complex is manipulated by a traveling wave force. See the Parton abstract and the immediately preceding paragraph.

Although Parton discloses protein as a moiety (col. 3:6-9), Parton does not mention having the protein non-specifically bind to the surface of a binding partner that is modified with a detergent. However, Parton clearly contemplates a variety of binding arrangements. See col. 3:25-45. Zhang, Hernandez, Rojas, and Youan discloses non-

specifically binding a protein to the surface of a binding partner that is modified with surfactant. It would have been obvious to non-specifically bind the protein to the surface of a binding partner that is modified with a detergent as taught by Zhang, Hernandez, Rojas, or Youan in the invention of Parton because then the protein and microparticle can be separated and recovered so that the microparticle can be use again fro a different sample and the proteins can be further processed and analyzed after the manipulation.

Addressing claim 38, Youan, Hernandez, and Zhang discloses SDS. Barring a contrary showing the choice or detergent, such as SDS is just optimization.

15. Claims 1-7, 12, 44, 68, and 69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fuchs et al. (US 5,948,231) ("Fuchs").

Addressing claims 1 and 44, Fuchs discloses a method for manipulating a moiety in a microfluidic application (abstract), which method comprises

a) coupling a moiety to be manipulated onto a surface of a binding partner of the moiety to form a moiety-binding partner complex (abstract); and

b) manipulating the moiety-binding partner complex with a physical force in a chip format, wherein the manipulation is effected through a combination of a signal source that is external to the chip and a structure that is built-in in the chip, thereby the moiety is manipulated (abstract; col. 4:20-33 although the location of the power source

is not mentioned there is no suggestion from the figures that it is part of the chip. Even if it is assumed to be located in the chip, to separate integral parts has been held obvious MPEP2144.04.V.C. Alternatively, it would have been obvious to one with ordinary skill in the art at eh time of the invention to have the power source (signal source) external to the chip so that it may be used different chips. This will save costs as on signal source can be used for a variety of chip configurations.), and wherein

the moiety is not directly manipulatable by an electrostatic force and the moiety binding partner complex is manipulated by an electrostatic force (inherent since claim 7 allows for the moiety to be protein or a nucleic acid and claim 12 allows for the binding partner to be a plastic particle. Fuchs discloses proteins and nucleic acids as moieties and polymer binding partners. See col. 8:15-37 and col. 21:45-50. Also note that Fuchs discloses a list of possible binding partners that overlaps those disclosed in Applicants' specification from the bottom of page 24 - top of page 25. Also, barring a contrary showing electrophoresis can be construed as an electrostatic force since one with ordinary skill in the art would understand it to be based on a fixed DC field, unless otherwise stated. See also col. 27:62-65, for example, which refers to a negative electrode).

Addressing claims 2-7, for the additional limitations of these claims see col. 8:15-38 and col. 8:51- col. 9:6. For claim 6 note that claim 5 does not require the molecule to be an inorganic molecule. The molecule could still be an organic molecule or a complex of an organic molecule and an inorganic molecule. Addressing claims 2-7, for the

additional limitations of these claims see col. 8:15-38 and col. 8:51 – col. 9:6. For claim 6 note that claim 5 does not require the molecule to be an inorganic molecule. The molecule could still be an organic molecule or a complex of an organic molecule and an inorganic molecule.

Addressing claim 68, Fuchs discloses a kit for manipulating a moiety in a microfluidic application, which kit comprises

a) a binding partner onto the surface of which a moiety to be manipulated can be coupled to form a moiety-binding partner complex (abstract);

b) means for coupling the moiety onto the surface of the binding partner (abstract and col. 8:15 – col. 15:20);

c) a chip on which the moiety-binding partner complex can be manipulated with a physical force that is effected through a combination of a signal source that is external to the chip and a structure that is built-in in the chip, thereby the moiety is manipulated ((abstract; col. 4:20-33 although the location of the power source is not mentioned there is no suggestion from the figures that it is part of the chip. Even if it is assumed to be located in the chip, to separate integral parts has been held obvious MPEP2144.04.V.C. Alternatively, it would have been obvious to one with ordinary skill in the art at eh time of the invention to have the power source (signal source) external to the chip so that it may be used different chips. This will save costs as on signal source can be used for a variety of chip configurations.), and wherein

the moiety is not directly manipulatable by an electrostatic force and the moiety binding partner complex is manipulated by an electrostatic force (inherent since claim 7 allows for the moiety to be protein or a nucleic acid and claim 12 allows for the binding partner to be a plastic particle. Fuchs discloses proteins and nucleic acids as moieties and polymer binding partners. See col. 8:15-37 and col. 21:45-50. Also note that Fuchs discloses a list of possible binding partners that overlaps those disclosed in Applicants' specification from the bottom of page 24 - top of page 25. Also, barring a contrary showing electrophoresis can be construed as an electrostatic force since one with ordinary skill in the art would understand it to be based on a fixed DC field, unless otherwise stated. See also col. 27:62-65, for example, which refers to a negative electrode).

Addressing claim 69, Fuchs discloses a method as required by claim 68. Although Fuchs does not mention providing instructions for coupling the moiety onto the surface of the binding partner and/or manipulate the moiety-binding partner complex on the chip, it would have been obvious to one with ordinary skill in the art at the time the invention was made to do so because then the operator of the kit will have to lose less time with trial and error experiments on how to use the kit.

16. Claims 72 and 73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weetall et al. (US 5,620,857) in view of Hawkins (WO 96/09379 A1) ('Hawkins"), CAPLUS abstract of Ma et al. ("Synthesis of uniform microspheres with higher content of 2-hydroxylmethacrylate by employing SPG (Shirasu porous glass) emulsification technique followed by swelling process of droplets," Journal of Applied Polymer Science (1997), 66(7), 1325-1341) ("Ma"), CAPLUS abstract of Chen et al. (CN 1145410 A), and CAPLSU abstract of Yang et al. ("New, porous microsphere of bisphenol A epoxy resin," Gaofenzi Xuebao (1997), (1), 119-120) ("Yang").

Addressing claims 72 and 73, for the claimed limitations see the abstract; Figure 1; col. 3:32-46; col. 3: 53-59; col. 4: 39-41; col. 5: 45-62; col. 6:15-23, col. 6:60-67 (competitive binding implies cleavable linkage), col. 7:63 – col. 8:3. Note that the structure comprising the cover slip (15) and well (17) at the top of Figure 1 can be construed as the chip of claim 1, the lens shown (but not labeled) in Figure 1 can be construed as the "structure that is built-in in said chip" of claim 1, and the laser of Figure 1 can be construed as the "signal source that is external to said chip." Also, Weetall specifically mentions using a "chip" format. See col. 7:63 to 8:1.

Although Weetall discloses DNA as a moiety and a bead as a binding partner (see Examples 7 and 8 in columns 7 and 8), Weetall does not mention having the binding partner be a porous bead and reversibly binding the DNA onto the surface of the bead in a buffer containing high salt concentration.

Hawkins discloses reversibly binding poilynucleotides, such as DNA, onto microparticles in a buffer having a high salt concentration. See page 3:25 – page 4:7

and page 3:20-24. It would have been obvious to one with ordinary skill in the art at the time of the invention to reversibly bind DNA, onto microparticles in a buffer having a high salt concentration as taught by Hawkins in the invention of Parton because then the microparticles can be recovered for use with a new sample and the DNA can be further processed or analyzed in a pure state (uncongugated) after the manipulation.

As for a porous bead, neither Parton nor Hawkins mention whether the bead is porous. However, they disclose that a wide variety of beads may be used (in Parton see col. 4:8-10 and in Hawkins see page 4:19-22) and a variety of porous microbeads were known at the time of the invention. See, for example, Yang, Chen, Ma. So, barring evidence to the contrary, such as unexpected results the choice of bead, such as a porous bead as taught by Yang, Chen, or Ma is just optimization. On with ordinary skill in the art at the time of the invention would select a bead that is compatible at least with the analyte it is to reversibly bind and the manipulating force. .

For claim 73 note that since the kit does not require a moiety parts (c) (i-iv) of the claim are only intended uses that do note further structurally limit the claim. In any event limitation (c)(ii) has been addressed in the rejection of claim 72.

Allowable Subject Matter

17. Claim 43 would be allowable if rewritten to overcome the rejection under 35 U.S.C. 112, 2nd paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

18. The following is a statement of reasons for the indication of allowable subject matter:

a) Claim 43 requires both (i) coupling a moiety to be manipulated onto a surface of a binding partner of the moiety to form a moiety-binding partner complex, and (ii) the moiety to be not directly manipulatable by an acoustic force and the moiety-binding partner complex to be manipulated by an acoustic force.

Weetall uses an optical radiation force. See the abstract.

Parton uses a dielectrophoresis force, such as a travelling-wave force. See the abstract.

Yasuda et al. (US 6,245,207) teaches acoustically separating cells in a non-complexed state. See the abstract. Yasuda et al. teaches away from forming a moiety-binding complex as Yasuda et al. states, "An object of the present invention is to provide a cell separation device for separating and collecting fresh cells having a charge effectively and continuously without dyeing by using competition between acoustic radiation force and electrostatic force.

[emphasis added]" See col. 2:22-27. Also, the moiety is clearly directly manipulatable by an acoustic force, which is contrary to what is required by claim 43.

Schram (US 4,743,361) teaches acoustically separating moieties, such as macromolecules cells, in a non-complexed state. See the abstract. The moieties are clearly directly manipulatable by an acoustic force, which is contrary to what is required by claim 43. See col. 4:29-65. Also, Schram does not disclose complexing the moieties with binding partners. Additionally, no part of the fluidic device of Schram is in a "chip" format, which as defined by Applicants "refers to a solid substrate with a single or a plurality of one-, two-, or three-dimensional micro structures on which certain processes, such as physical, chemical, biological, biophysical or biochemical processes, etc., can be carried out. See the bottom of page 19 of the specification and col. 9:60-68 in Schram.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ALEX NOGUEROLA whose telephone number is (571) 272-1343. The examiner can normally be reached on M-F 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, NAM NGUYEN can be reached on (571) 272-1342. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Alex Noguerola
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AU 1753
June 17, 2005